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The Clinical Value of the Systemic Inflammatory Response Syndrome (SIRS) in Abdominal Aortic Aneurysm Repair

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Objectives. The systemic inflammatory response syndrome (SIRS) is common after major surgery. We examine the dynamics of SIRS in AAA patients, and assess the impact of the number of SIRS criteria on patient outcome.

Design. Prospective study of 151 consecutive patients with AAA, undergoing repair electively, urgently or with rupture.

Methods. SIRS scores and organ failure scores were recorded prospectively each day for all patients. Outcome measures included length of stay, evidence of organ failure and mortality.

Results. The majority of patients developed SIRS postoperatively. Elective patients with a cumulative SIRS score of ≥ 10 during postoperative days 1–4 were more likely to die, compared to patients with a SIRS score of < 10 ($p = 0.02$). The development of SIRS late in the postoperative period (day 5–10) was associated with adverse outcome (death) in elective patients ($p = 0.01$). The actual number of SIRS criteria present did not significantly correlate with either outcome or the incidence of organ failure.

Conclusions. SIRS is common in patients undergoing AAA repair. The SIRS score provides useful information regarding a patient's physiological state. High SIRS scores, and the development of SIRS late in the postoperative period are associated with adverse outcome in elective patients, and can therefore be used as an indicator of potential problems.

Key Words: Abdominal aortic aneurysm; Systemic inflammatory response syndrome.

Introduction

The systemic inflammatory response syndrome (SIRS) was first defined in 1991 at the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference.¹ SIRS should be regarded as a physiological state rather than a specific diagnosis.² It forms part of the acute inflammatory response, and is thought to be mediated by the presence of circulating inflammatory mediators such as the cytokines interleukin-1 (IL-1), interleukin-6 (IL-6) and tumour necrosis factor- α (TNF α).³

By convention, SIRS is defined using four clinical criteria as described in Table 1. The concurrent presence of two or more of these criteria constitutes SIRS. Therefore, a patient with either two, three or four criteria to match those of Table 1, is defined as having SIRS.

If SIRS arises in association with a documented infection, a patient is described as having 'sepsis'. SIRS or sepsis may then be complicated by organ failure,

giving either single organ failure (SOF) or multiple organ failure (MOF) depending on the number of organs failed. MOF is defined by the failure of two or more organ systems for a period of at least 24 h.

Therefore, SIRS encompasses a wide clinical spectrum, from that of a well patient on one hand with minor physiological derangement, to that of a patient with MOF at the other extreme,⁴ with SIRS occurring early in the chain of events. This philosophy has led researchers to examine links between SIRS and MOF, and to see whether the presence of SIRS may predict the development of organ failure.⁵ In patients that have undergone AAA repair, SIRS occurs before MOF in the majority of cases. The resolution of both SIRS and organ failure at any point during the postoperative period after AAA repair has been shown to be a useful prognosticator of successful outcome.⁶

Although the diagnosis of SIRS in essence is very straightforward, the extrapolation to the impact that it may have on an individual patient is unclear. It is also unclear, whether the total number of SIRS criteria actually present rather than merely the presence or absence of SIRS has any influence on patient outcome after abdominal aortic aneurysm surgery. For example, patients that have either two, three or four SIRS criteria

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Table 1. The four criteria for the definition of SIRS. SIRS is defined by the presence of two or more of the following criteria

SIRS criteria
A white cell count of $>12,000$ cells/mm ³ , or <4000 cells/mm ³ , or $>10\%$ immature (band) forms
A temperature of >38 °C or <36 °C
A heart rate of >90 beats per minute
A respiratory rate of >20 breaths per minute, or PaCO ₂ <4.3 kPa

present all have SIRS, but is one more likely to have a worse outcome?

This paper expands on work previously conducted within our department,⁶ by further investigating the presence of SIRS in a larger number of AAA patients, and by specifically examining both the timing and the relevance of the number of SIRS criteria within the clinical setting. We aim to explore whether the use of a modified SIRS score generated by tightening the definition of SIRS (so that SIRS is defined only when either three or four criteria are present) can predict outcome and organ failure more effectively in AAA patients postoperatively.

Methods

A total of 151 consecutive patients undergoing AAA repair between October 2000 and April 2002 were prospectively recruited. Inclusion criteria consisted of any patient undergoing AAA repair either electively (EAAA), urgently (UAAA), or having repair of a ruptured aneurysm (RAAA). There were no exclusion criteria. An urgent case was defined as an aneurysm in which the patient was symptomatic, e.g. presenting with back pain, and which was repaired within 24 h of admission. A ruptured aneurysm was defined by the presence of intra-peritoneal blood and/or retroperitoneal haematoma at laparotomy.

All patients were followed-up daily to record the number of SIRS criteria. Patients were given a SIRS score of 0, 1, 2, 3 or 4 on each day depending on the number of SIRS criteria present. For scoring, the methodology originally described by Bone *et al.*¹ was used. To calculate mean daily SIRS scores for each group, the SIRS scores for each patient in the group were added up on each day, and then divided by the number of patients in the group. The presence of any organ failure as described by Knaus *et al.*⁷ (Table 2) was also documented. Other outcome measures observed included mortality, length of hospital stay and lengths of stay on the surgical ward and critical care unit (intensive care unit (ITU: level-3) or high dependency unit (HDU: level-2)).

In order to refine the outcome measures for data

analysis in the elective group, variables were further divided as follows. Hospital stay was divided into an 'early' hospital period (day 1–4) and a 'late' hospital period (day 5–10). A 'long' ITU stay was designated as more than 3 days. This was because the majority of elective and urgent patients with uncomplicated postoperative recoveries had been discharged from ITU by this time. A 'long' hospital stay was defined as more than the mean hospital stay (in days) for each particular group, again as the majority of patients experiencing an uncomplicated recovery had been discharge by this time.

All statistical analyses were performed using SPSS version 11.0. *p*-Values of less than 0.05 were considered to be statistically significant. The specific statistical test performed is shown in brackets after the *p*-value. For comparison of means, Student's *t*-test was used, where the data were normally distributed, and the Mann–Whitney U-test was used when data were not normally distributed. For comparison of proportions, a Chi-squared test (χ^2) was used unless the expected frequency in any one cell was less than five, whereby, Fisher's exact test was used. Data were assumed to be normally distributed, if the skewness value given by SPSS was less than twice its standard error.

Results

Patient demographics

One hundred and fifty-one patients were recruited. One hundred patients underwent elective AAA repair, 35 had ruptured aneurysms and 16 underwent urgent repair. The median age of all patients was 71.6 years (range 48–85). 82.8% of patients were male ($n = 125$). 84.1% ($n = 127$) gave a positive smoking history. All patients were Caucasian, except one patient from the Indian subcontinent and one from the Middle East. The overall mortality was 13.9% ($n = 21$). Mortality in the elective group was 5% ($n = 5$), 6.3% in the urgent group ($n = 1$) and 42.9% in the rupture group ($n = 15$). Due to the small numbers in the urgent group, this group is no longer discussed.

Elective AAA

Eighty-nine percent ($n = 89$) of elective patients developed SIRS at some point during their hospital stay. The majority (54%) of these patients, however, only experienced SIRS during the first three post-operative days (Fig. 1), and tended to have lower SIRS scores rather than SIRS scores of 3 or 4 (Fig. 2). Elective

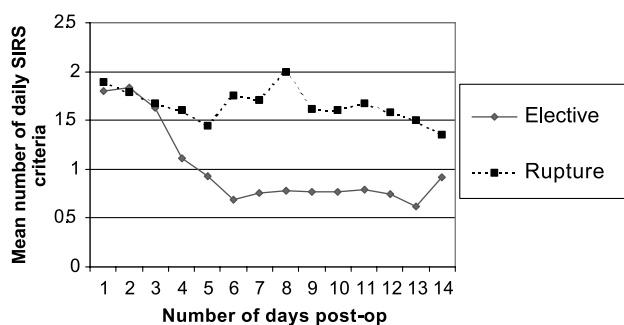
Table 2. Definitions of organ failure according to Knaus *et al.*⁷ One or more positive variables in each category during a 24 h period constitutes that organ failing on that day

Organ system	Criteria for failure
Cardiovascular	Heart rate ≤ 54 beats/minute Mean arterial pressure ≤ 49 mmHg Ventricular tachycardia or ventricular fibrillation
Respiratory	pH ≤ 7.24 and $\text{PaCO}_2 \leq 49$ mmHg (6.57 kPa) Respiratory rate ≤ 5 breaths/minute or ≥ 49 breaths/minute $\text{PaCO}_2 \geq 50$ mmHg (6.58 kPa) $\text{A}_a\text{DO}_2 \geq 46.5$ Dependent on ventilator on 4th organ failure day (i.e. not applicable until after 72 h organ failure)
Renal (unless on chronic dialysis prior to admission)	Urine output < 480 ml/24 h or < 160 ml/8 h Serum urea ≥ 16.6 mmol/l Serum creatinine ≥ 308 $\mu\text{mol/l}$
Haematological	Leukocyte count $\leq 1 \times 10^3/\text{mm}^3$ Platelet count $\leq 20 \times 10^3/\text{mm}^3$ Haematocrit $\leq 20\%$
Neurological	Glasgow coma scale ≤ 6 (in absence of any sedation at any one point in day)

A_aDO_2 , alveolar-arterial oxygen difference.

patients that died tended to have a prolonged and higher mean daily SIRS score compared to survivors during the first 14 postoperative days (Fig. 3). Non-survivors had a higher mean SIRS score (2.19 of a maximum possible score of 4) during their hospital admission time than survivors (0.95) ($p < 0.01$ Student's *t*-test, 95% confidence interval of the difference -1.61 to -0.81).

In the elective group, it was noted that the mean SIRS score decreased rapidly in the first 4 days after admission (Fig. 1). In order to determine, whether patients with a high SIRS score in the first 4 days were more likely to have an adverse outcome, patients were dichotomised by taking 50th centiles of the mean SIRS score for the first four postoperative days. When analysed, there was no positive correlation with adverse outcome in patients with high early SIRS scores, but was significant if a patient had a cumulative SIRS score (calculated by adding the daily SIRS scores) of 10 or more during the first four postoperative days ($p = 0.02$ Fisher's exact test). Patients

**Fig. 1.** Line graph demonstrating the change in the mean number of SIRS criteria on each postoperative day for elective and rupture patients.

were also subdivided into those who had a SIRS score of 3 or 4 at any point during the first 4 days, and those that only had a SIRS score of 2 or no SIRS at all. No significant differences in outcome (mortality) existed in any group.

As the majority of elective patients experienced a reduction in their mean SIRS score over the first 4 days, the impact of having a persistently high SIRS score, continuing into and during the 5th–10th day of admission was investigated. Elective patients were dichotomised by taking the 50th centile of the mean cumulative SIRS score (mean = 3.8) for the 5th–10th postoperative days. Patients with a SIRS score of greater than the mean were again found to be significantly more likely to die ($p = 0.02$ Fisher's exact test).

The significance of the actual number of SIRS criteria was also of interest during this later time-period. Elective patients that demonstrated SIRS at any time on day 5–10, were significantly more likely to die ($p = 0.01$ Fisher's exact test). With regard to specific SIRS criteria, the influence of having either two, three or four criteria on any day had no influence on outcome ($p = 0.63 \chi^2$).

With regard to ITU and ward admission time, elective patients experienced a mean ITU stay of 0.66 days (standard deviation 3.10 days) and a total hospital stay of 12.75 days (standard deviation 9.90 days).

Elective patients with a long ITU stay (e.g. more than 3 days) had a higher mean SIRS score (1.78) than patients with a short ITU stay (0.99) ($p = 0.01$ Student's *t*-test, 95% confidence interval of the difference -1.41 to -0.17). Patients with a long ward stay had no difference in mean SIRS score than patients with a

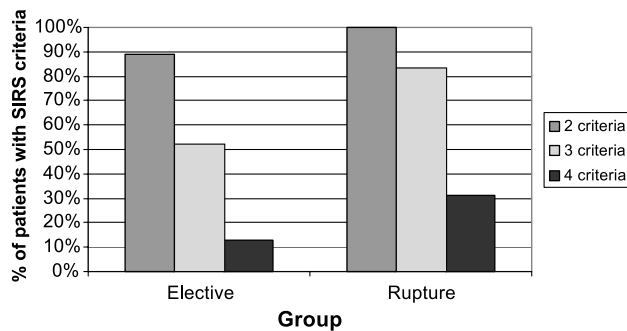


Fig. 2. Bar chart demonstrating the number of elective and rupture patients (expressed as a percentage) to score either 2, 3 or 4 SIRS criteria at any time during admission.

short ward stay (1.05 compared with 0.97 ($p = 0.5$ Student's t -test, 95% confidence interval of the difference -0.14 to 0.29). Patients that had a higher SIRS score (e.g. 3 or 4) at any time had no difference in hospital stay compared to those with a lower SIRS score (13.71 days *versus* 11.71 days ($p = 0.32$ Student's t -test, 95% confidence interval of the difference -5.94 to 1.93). Elective patients that developed SIRS late in the postoperative period (days 5–10) had a significantly longer ward stay compared to patients that did not (16.37 *versus* 10.94 days), ($p = 0.02$ Student's t -test, 95% confidence interval of the difference -10.13 to -0.74) (Fig. 4).

Regarding MOF, patients with SIRS scores of 3 or 4 during the first four postoperative days had a higher incidence of MOF. Only one patient out of 51 with a SIRS score of 2 developed MOF, compared to six out of 49 patients with SIRS scores of 3 or 4. Although suggesting a trend, these results, however, were not of statistical significance ($p = 0.06$ Fisher's exact test).

Ruptured AAA

All of the 35 rupture patients developed SIRS post-

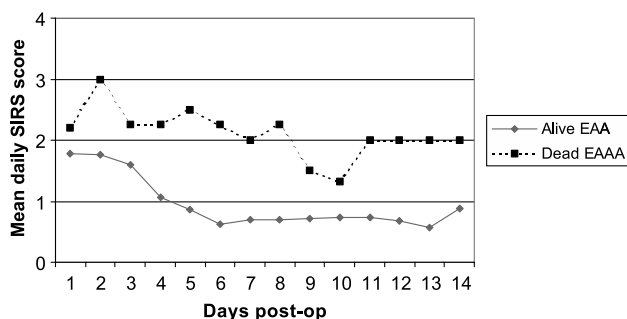


Fig. 3. Line graph for elective patients (EAAA) demonstrating the change in the mean number of daily SIRS criteria in survivors and non-survivors, during the first 14 postoperative days.

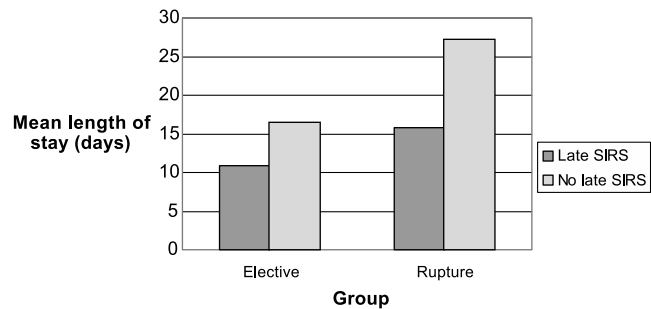


Fig. 4. Bar chart demonstrating the mean length of hospital stay in elective and rupture patients with or without late SIRS.

operatively. These patients demonstrated prolonged SIRS postoperatively, compared to EAAA and UAAA patients (Fig. 1). A higher percentage of patients demonstrated high SIRS scores: 83% of RAAA patients had three criteria present at any time compared to 52% of EAAA patients, and 31% of RAAA patients had four criteria present compared to only 13% of elective patients (Fig. 2). These frequencies differed significantly from those of other groups ($p = 0.03$ χ^2). RAAA patients that survived had a very gradual decrease in their mean SIRS score during the first 14 days postoperatively, whereas non-survivors experienced an increased and prolonged change in their mean SIRS score after the fifth postoperative day (Fig. 5). The non-survivors had a statistically higher mean SIRS score (2.06) during this time compared to the survivors (1.37) ($p < 0.01$ Student's t -test, 95% confidence interval of the difference -1.22 to -1.89). However, when examining the significance of individual SIRS criteria *per se*, no difference in survival existed between patients depending on whether they had either two, three or four criteria present during this time.

With regard to length of hospital stay, ruptured patients had a mean ITU stay of 9.86 days (standard deviation 11.48) and a hospital stay of 23.97 days (standard deviation 18.57). Patients that stayed longer

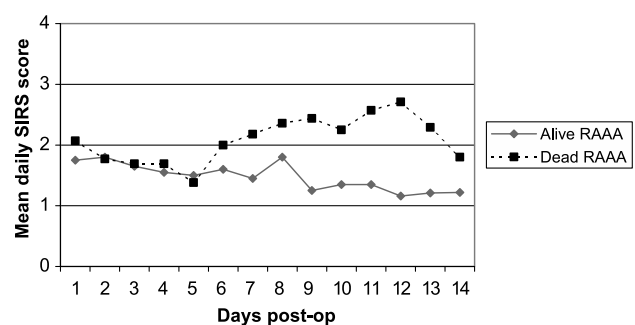


Fig. 5. Line graph for rupture patients demonstrating the change in the mean daily SIRS score for the group, in survivors and non-survivors over the first 14 days.

than the mean length of stay for the group had a higher mean SIRS score (mean of 1.76) during admission than patients with a hospital stay of less than the mean (mean of 1.26) ($p = 0.04$ Student's *t*-test, 95% confidence interval of the difference 0.03–0.97). The individual number of SIRS criteria present did not correlate with length of stay.

With regard to organ failure, 34 patients (97%) developed failure of one organ system, and 21 patients (60%) developed MOF. The number of patients with MOF increased as the definition of SIRS was tightened to three or four criteria, although this did not reach statistical significance ($p = 0.85 \chi^2$) (Fig. 6).

Discussion

The aim of this paper has been to explore whether the timing of SIRS and the modification of the SIRS scoring system by tightening the definition of SIRS (to either three or four criteria) could be used to predict outcome and organ failure in AAA patients. The SIRS score was chosen specifically as it is a scoring system that is both quick and easy to perform at the bedside.

Overall, no correlation was found between the precise number of SIRS criteria and mortality, admission time or organ failure, e.g. a patients that had SIRS with two criteria was no more likely to have an adverse outcome than a patient with SIRS that had all four criteria present. However, when the data was explored in more detail, the timing of the occurrence of SIRS was found to be important. The potential for the importance of the timing of the development of SIRS was identified as being of potential significance in response to the observation that the mean daily SIRS score in elective patients quickly reduced over time in patients that survived postoperatively compared to those that died. It was found that elective patients with very high cumulative SIRS scores (i.e. ≥ 10) in the first

four postoperative days were more likely to die. This indicates that high SIRS scores for a number of days in the early postoperative period are a significant predictor of death, whereas having isolated days with a high SIRS score of 3 or 4 is not. This would seem to indicate that if a patient was able to quickly recover from a short period (i.e. 1 or 2 days) of high-scoring SIRS they were likely to have a successful outcome, whereas if they did not make a swift physiological recovery with rapid reversal of their proinflammatory state, they were significantly more likely to die. This is not reproduced in the rupture group as the majority of patients experience very high early SIRS scores, whether they survive or not.

Examining the data on the late development of SIRS, elective mortality was significantly higher in patients with a SIRS score greater than the mean (3.8) during days 5–10. Mortality in elective patients was not influenced by the peak SIRS score (i.e. 2, 3 or 4) during this late time period, but the presence of SIRS *per se* was significantly associated with death. This therefore implies that it is the development of late SIRS in itself, rather than the number of actual SIRS criteria that is important in the prediction of postoperative deaths in EAAA patients.

Finally, it was of interest to investigate whether the presence or persistence of SIRS predicted those patients who may experience a more protracted postoperative course and prolonged stay. Neither the presence of early SIRS (day 1–4), nor high early SIRS scores (3 or 4) influenced the length of hospital stay in any group. The presence of late SIRS (day 5–10), however, did significantly increase hospital stay in elective and urgent patients. This is to be expected as the majority of patients demonstrate SIRS in the early postoperative period as a physiological response to surgery. However, by day 5, those patients which have either not undergone resolution of their SIRS or who develop late SIRS will be either experiencing an abnormally prolonged inflammatory response or the development of postoperative complications. We do, however, accept that the number of deaths in the elective group was low.

It is accepted that there is a continuum from the development of SIRS to the onset of sepsis and progression to septic shock and multiple organ dysfunction.⁴ The development of SIRS in a patient should therefore be taken as a warning that the patient is at risk of impending organ failure and its appreciable associated mortality. Previous research into the clinical implications of SIRS is not widespread. A prospective study by Rangel-Frausto *et al.*,⁵ was really the first to look at the epidemiology of SIRS and its relationship to sepsis, severe sepsis and septic shock in

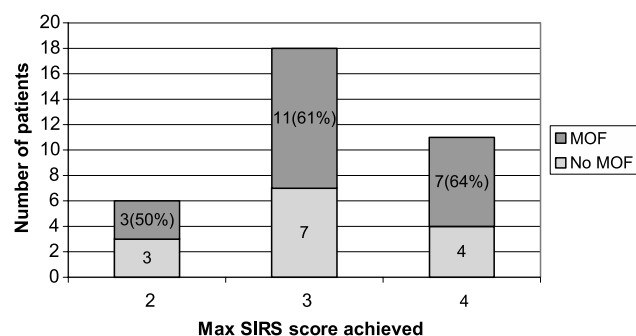


Fig. 6. Bar chart displaying the incidence of multiple organ failure (MOF) in rupture patients with increasing SIRS scores.

ITU and ward patients. They demonstrated not only that there was a relationship between SIRS, sepsis and septic shock, but also that the median interval from the development of SIRS to the development of sepsis was inversely correlated with the number of SIRS criteria present, thereby also being the first to imply the significance of the actual SIRS score. Other authors, however, have not found SIRS to have such a useful predictive value. Pittet *et al.*⁸ in a study of surgical ICU patients found SIRS to be unhelpful in predicting sepsis and septic shock due to its high prevalence and resultant lack of specificity. Smail *et al.*⁹ also concluded SIRS as a means of predicting MOF in trauma patients to be unreliable. However, this study was retrospective, and the precise timings of the development of SIRS and MODS are unclear. Pittet is not the only author to criticise the lack of specificity of SIRS: Salvo *et al.*¹⁰ stressed the important point that conditions such as anxiety, pain and slight hypovolaemia (which are frequently observed after elective surgery), may lead to increased heart and respiratory rates in the absence of a true systemic inflammatory response. This point is important in any study evaluating SIRS.

The lack of consensus regarding the predictive value of SIRS may arise from the lack of patient homogeneity in some of the previous studies. Our study demonstrates large differences in the natural history of SIRS between patient groups (RAAA and EAAA), and the subsequent possible misinterpretation of the data as a result. Our data would therefore indicate that for reliable interpretation of future data (especially where small studies are concerned), there should be of a high degree of homogeneity between patients. This appears to correlate with previous research, in which studies looking at specific groups of patients; namely trauma patients,^{11–14} patients undergoing abdominal surgery,¹⁵ obstetric patients¹⁶ and patients with subarachnoid haemorrhage¹⁷ found SIRS to be of use for the prediction of adverse outcomes.

Criticisms of the lack of specificity of SIRS^{9,10,18,19} further begs the question of whether by tightening the definition of SIRS (e.g. to SIRS being present with only three of four criteria), the specificity and subsequent clinical usefulness can be increased. Our research has addressed this question with specific regard to patients undergoing AAA repair.

This paper has demonstrated that the SIRS is commonly seen in patients undergoing AAA repair. Scoring patients for SIRS proved to be a fast and simple task to perform as a bed-side assessment of clinical state, helping to focus the observer towards the physiological state of the patient, and if present should

alert the observer to the possibility of underlying pathologies as a cause for SIRS.

In conclusion, the individual SIRS score could not be used to predict outcome or organ failure in patients after AAA repair. However, in elective patients, it appears that rather than the actual numerical value of the SIRS score, it is the timing of the development of SIRS (e.g. SIRS days 5–10), and the presence of SIRS for prolonged periods that are significant predictors of adverse outcome.

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